REMARKS

Claims 1-11, 17-18, and 20-30 remain pending in this application after entry of the above amendment. Applicants submit that the amendments to claims are fully supported by the application as originally filed. In particular, Applicants submit that the amendment to Claim 1 is supported by lines 20-33 of the specification. No new matter has been added by the above-described amendments. Furthermore, any amendment or cancellation of the claims is made without prejudice to the prosecution of such subject matter in this or other patent applications.

Claim Objections

The Examiner has objected to Claim 14 as including an improper status identifier. Applicants submit that, in light of the amendment presented above, the Examiner's objection has been rendered moot and therefore withdrawal of that objection is respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph, enablement

The Examiner has rejected claims 1-11, 14, 17-18, and 20-30 under 35 U.S.C. §112, first paragraph, as allegedly failing to enable a person skilled in the art to make and/or use the invention commensurate in scope with the claims. In particular, the Examiner argues that because the claims are directed to sequences that may have one or more amino acid substitutions ("functional homologues"), the claims encompass in their breadth a variety of sequences which cannot be sufficiently predicted due to the specification's alleged lack of guidance regarding acceptable amino acid substitutions, additions, or deletions.

As a preliminary matter, Applicants note that Claim 14 has been canceled and therefore the rejection of that claim has been rendered moot. Furthermore, although Applicants do not acquiesce in the propriety of the Examiner's position that claims directed to functional homologues of the specifically claimed SEQ ID NOs fail to be enabled by the instant specification, Applicants have amended the claims to remove the phrase "functional homologues." Accordingly, Applicants respectfully submit that the Examiner's basis for rejecting the instant claims has been rendered moot and withdrawal of the rejection is requested.

The pending claims are fully supported by an enabling disclosure. Patent claims are enabled so long as they do not require experimentation to practice them. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation.[1] Having the instant specification in hand, a person having ordinary skill in the art would not be required to engage in undue experimentation to practice the invention recited in the amended claims.

As discussed in the Response of October 26, 2007, the instant specification provides ample disclosures of binding domains with amino acid sequences that have the ability to bind to PsaA protein (See Figures 16-18). A person of ordinary skill in the art would not have to "predict" which substitutions would result in an antibody capable of specifically binding PsaA protein. Instead, the skilled artisan would be able to employ the disclosed and other routine methods that are described in the specification or are otherwise known in the art to identify substitutions of the disclosed sequences that fall within the scope of the claims.

It is stated in the office action that "[s]elective point mutations to one key residue could eliminate the function of the polypeptide." While Applicants do not dispute this statement, Applicants note that the amended claims are enabled because a person having ordinary skill in the art would employ the disclosed and other routine methods to identify binding domains having a single amino acid substation that can bind PsaA. Any protein derived from the claimed sequences that are incapable of binding to pneumonia surface adhesion A protein would not fall within the scope of the claims.

It is also stated in the office action that the "claims allow for as great as 40% variation or even more, e.g., homologues of SEQ ID NO:4 or 6" and that it is "expensive and time consuming to make amino acid substitutions at more than one position… ." These alleged grounds for rejection for lack of enablement have been rendered moot because the "functional homolog" language has been deleted and the claims recite single amino acid substitutions.

[1] See, M.P.E.P. § 2164 citing *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom. Massachusetts Institute of Technology v. A. B. Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed Cir 1983).

Furthermore, the fact that experimentation is "expensive" or "time consuming" does not necessarily render it undue.[2]

As evidenced by the instant specification and exhibits 1-7[3], skilled artisans were readily able to make and use binding polypeptides comprising binding domains of SEQ ID NOs: 4 and 6, or variants of those binding domain sequences having single amino acid substitutions, which specifically bind to the same antigen as the parent binding polypeptide. Thus, the instant application in combination with the state of the art at the time the application was filed teaches persons of ordinary skill in the art how to make and use the claimed invention without undue experimentation. In light of the foregoing, Applicants request reconsideration and withdrawal of the instant rejection.

Rejections under 35 U.S.C. §112, first paragraph, written description

The Examiner has rejected claims 1-11, 14, 17-18, and 20-30 under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner argues that the specification fails to adequately describe the full scope of functional homologues of SEQ ID NOs 4 and 6.

As pointed out by the Examiner, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species.[4] Example 14 of the Synopsis of Application of Written Description Guidelines issued by the U.S. Patent Office clearly states that protein variants can meet the requirements of 35 U.S.C. §112, first paragraph, even if the specification contemplates but does not exemplify variants of the protein if (1) the procedures for making such variant proteins are routine in the art, (2) if the specification provides an assay for detecting the functional activity of the protein, and (3) the variant has some sequence relationship to the original sequence.

---

[2] See, United States v. Telectronics Inc., 857 F.2d 778, 785 (Fed Cir 1988), "Finally, the emphasis by the district court on the time and cost of such [experimentation] is misplaced. While these factors may be taken into account, in the circumstances of this case we are unpersuaded that standing alone they show the experimentation to be excessive."

[3] See pages 9-12 of the Response Filed October 26, 2007.

[4] See Fed. Reg., Vol. 66, No. 4, pages 1099-1111 (2001).

Applicants first note that Claim 14 has been canceled and therefore the rejection of that claim has been rendered moot. Furthermore, although Applicants again do not acquiesce in the propriety of the Examiner's position that claims directed to functional homologues of the specifically claimed SEQ ID NOs were not sufficiently described in the instant specification, Applicants point out that the claims have been amended and no longer recite functional homologues. Accordingly, Applicants respectfully submit that the Examiner's basis for rejecting the instant claims has been rendered moot and withdrawal of the rejection is requested.

The instant specification discloses a representative number of species that fully supports the amended claims. Specifically, procedures for making such variant proteins are disclosed and are routine in the art[5] and the specification has provided an assay for detecting the functional activity of the protein (see Examples 2-4 of the instant specification which describe various PsaA binding assays). Moreover, the variant must have some sequence relationship to the original sequence (incorporation of SEQ ID NOs: 4 and 6, or variants having no more than a single amino acid substitution in each).

Given the correct standard as outlined above and the teachings of the specification, Applicants respectfully submit that the claimed genus is fully supported by the specification so as to convey to one skilled in the art that Applicants were, in fact, in possession of the claimed invention at the time the application was filed. Based on all of the foregoing, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Rejections under 35 U.S.C. §102(b)

The Examiner has rejected Claims 1-5, 10-15, and 17-23 under 35 U.S.C. §102(b) as allegedly anticipated by Korman et al. (WO 200114424) in light of Hoogenboom (TIBs, 1997, vol 15, 62-70). In particular, the Examiner argues that Korman et al. teach an antibody having a sequence 100% identical to SEQ ID NO: 6 and thus the claims are inherently anticipated by that disclosure, regardless of whether Korman et al. teach the ability of that sequence to bind PsaA.

Applicants respectfully traverse the foregoing rejection and assert that the instant claims are not anticipated by the cited art. A proper rejection of the claims requires the

[5] See the discussion of Exhibits 1-7 on pages 9-12 of the October 26, 2008 Response.

Examiner to show that each and every element as set forth in the claim is found, either expressly or inherently, in the asserted reference.[6] This has not been done.

The cited art does not expressly or inherently disclose every element of the pending claims. In particular, we note that the Examiner has relied on the incorporation of the term "functional homologues" to argue that the cited art teaches a sequence that could be considered equivalent to the second binding domain of the claimed binding polypeptide. [7] Although Applicants do not acquiesce in the propriety of the Examiner's position that claims directed to functional homologues of the specifically claimed SEQ ID NOs would support such a rejection, Applicants note that the term has been removed from the pending claims. In light of this amendment to the claims, Applicants submit that the basis for this rejection has been rendered moot and therefore withdrawal of the instant rejection is respectfully requested.

As conceded by the Examiner, the cited art does not disclose SEQ ID NO: 4. Applicants submit that the art also fails to disclose any variant thereof having a single amino acid substitution. Accordingly, the cited art does not disclose a binding polypeptide having two binding domains where the first comprises SEQ ID NO: 6, or variant thereof having a single amino acid substitution, and said second binding domain comprises the amino acid sequence of SEQ ID NO: 4, or variant thereof having a single amino acid substitution. Since each and every element of the pending claims is not found in the cited art, as required under 35 U.S.C. § 102(b), Applicant submit that the instant claims are in allowable format and the pending rejections should be withdrawn.

The Examiner has also rejected Claims 1-7, 10, 17, 22, 24, 29, and 30 under 35 U.S.C. §102(b) as allegedly anticipated by one of Crook et al., (Clin Diagn Lab, 1998), Srivastava et al., (Hybridoma, 2000), or Gor et al., (Infect. Immun 2002, vol 70, 5589-95), in light of Hoogenboom. In particular the Examiner argues that the rejected claims are sufficiently broad that the generic PsaA binding disclosures of Crook et al., Srivastava, and/or Gor et al., could be combined with Hoogenboom to anticipate the instant claims.

---

[6] See, Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference."

[7] See Page 9 of the instant Office Action, "The Examiner agrees that Korman et al. do not disclose of a CDR comprising SEQ ID NO: 4..."

As pointed out above, a proper rejection of the claims requires the Examiner to show that each and every element as set forth in the claim is found, either expressly or inherently, in the asserted reference. This has not been done. The rejection relies upon the term "functional homologues" as a basis for rejecting the instant claims over the cited art. The cited art, however, does not disclose a sequence that is identical to SEQ ID NO: 4 or a variant thereof having a single amino acid substitution. Although Applicants do not acquiesce in the propriety of the Examiner's position that claims directed to functional homologues of the specifically claimed SEQ ID NOs would support such a rejection, Applicants note that the term has been removed from the pending claims. In light of this amendment to the claims, Applicants submit that the basis for this rejection has been rendered moot and therefore withdrawal of the instant rejection is respectfully requested.

Because the cited art does not expressly or inherently disclose every element of the amended claims, it cannot anticipate them under 35 U.S.C. § 102(b). Thus, reconsideration and withdrawal of the instant rejection is requested.

Rejections under 35 U.S.C. §103(a)

Claims 6-9, 20-21, and 23 stand rejected under 35 U.S.C. §103(a) as unpatentable over Srivastava et al. or Korman et al. in view of Kriangkum et al., (Biomolecular Engineering, 2001, vol 18, 31-34) further in view of Hoogenboom. Applicants respectfully point out that the examiner has not met his burden of establishing a prima facie case of obviousness. The Examiner must establish that one of skill in the art would have a reasonable expectation of success in obtaining the binding polypeptides encompassed by the pending claims and, in particular, as currently drafted. This has not been done.

Applicants assert that, as set forth in Graham v. J. Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), there are several steps that must be followed in order to properly establish an obviousness rejection under 35 U.S.C. § 103. First the scope and content of the prior art are to be determined, then any differences between the prior art and the claims at issue are to be ascertained, and finally the level of ordinary skill in the pertinent art is resolved. It is against this background that the obviousness or nonobviousness of the subject matter is determined by identifying whether one of ordinary skill in the art would have a reasonable expectation of

success in achieving the claimed invention by making the proposed combination.[8] Although the Supreme Court has asserted that these "Graham Factors" are to be analyzed in a flexible manner, taking into consideration the common knowledge and common sense of those of ordinary skill in the art, Applicants note that the Court specifically stated that the above-described factors are consistent with an appropriate test for establishing obviousness.[9]

Applicants point out that the "functional homologues" element on which the Examiner's rejection is based has been deleted, rendering the instant rejection moot. The instant claims are now directed to binding polypeptides comprising at least a first and a second binding domain capable of specifically binding PsaA protein, said first binding domain comprises the amino acid sequence of SEQ ID NO 6, or a variant thereof having a single amino acid substitution, and said second binding domain that comprises the amino acid sequence of SEQ ID NO: 4, or variants thereof having a single amino acid substitution. The Examiner has not established how one of skill in the art would obtain binding polypeptides having such specific sequences based on the cited art. At best, these references may suggest that making a broad genus of binding polypeptides could be tried, however, "obvious to try" is not the applicable standard here. While *KSR v. Teleflex* suggests that "obvious to try" may be an acceptable basis for finding obviousness in some circumstances,[10] it does not apply in situations such as this one. Here, there is a large number of possible sequences and significant unpredictability in the art. Thus the cited references provide no reasonable expectation of success in obtaining the binding polypeptides encompassed by the pending claims.[11] Therefore, the cited references do not render the instant claims obvious.

In light of the foregoing, Applicants respectfully submit that the Examiner has failed to establish a prima facie case of obviousness and therefore withdrawal of the instant rejection is respectfully requested.

---

[8] M.P.E.P. §2143; *In re* Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986)
[9] *KSR v. Teleflex*, 127 S. Ct. 1727, 1734 (2007)
[10] Id at 1732, "When there is a design need or market pressure to solve a problem and ***there are a finite number of identified, predictable solutions***, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp." [emphasis added].
[11] *Takeda Chem. Indust.. v. Alphapharm LTD.*, 492 F.3d 1350 (Fed. Cir., 2007)

Conclusion

Entry of the foregoing amendments and remarks into the file of the above-identified application is respectfully requested. Applicants believe that the invention described and defined by Claim 1-11, 17-18, and 20-30 are in condition for allowance. Withdrawal of all rejections and reconsideration of the amended claims is requested. An early allowance is earnestly sought.

To expedite allowance of this application, the Examiner is invited to telephone the undersigned if the Examiner believes a telephone call would be helpful in advancing prosecution.

Respectfully submitted,

Dated: 4/14/08

Steven P. Lendaris
Reg. No. 53,202
Attorney for Applicants

BAKER BOTTS L.L.P.
Customer No. 63367
30 Rockefeller Plaza
New York, NY 10112-4498
(212) 408-2500